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Running Head: Pharmacokinetic Modeling for Study Design

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Abbreviations:

NRC	National Research Council
MNCPES	Minnesota Children's Pesticide Exposure Study
PK	pharmacokinetic
EPA	United States Environmental Protection Agency
SD	Standard Deviation

Outline of Manuscript Section Headers:

ABSTRACT

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ABSTRACT

Validating an exposure pathway model is difficult because the biomarker, which is often used to evaluate the model prediction, is an integrated measure for exposures from all the exposure routes and pathways. The purpose of this paper is to demonstrate a method to use pharmacokinetic (PK) modeling and computer simulation to guide the design of field studies to validate pathway models. The children's dietary intake model was discussed in detail as an example. Three important aspects were identified for a successful design to evaluate the children's dietary intake model: (1) longitudinally designed study with significant changes in the exposure for the route/pathway of interest; (2) short biological half-life of the selected chemical; and (3) sufficient loading of the selected chemical at sufficient levels. Using PK modeling to guide a study design allowed a path-specific exposure model to be evaluated using urinary metabolite biomarkers.